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Gender related Long-term Differences after Open Infrainguinal Surgery for Critical Limb Ischemia

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WHAT THIS PAPER ADDS

The gender related disparity in critical limb ischemia outcomes has been clearly emphasized, highlighting the need for further and longer follow-up investigations, and justifying the recent call to action concerning women and peripheral arterial disease by the American Heart Association, which is why critical limb ischemia and open infrainguinal surgery in women have been focused on. The results show worse immediate and long-term outcomes in women, justifying intensive care in pre-operative period, but also better follow up.

Objective: The role of gender on long-term infrainguinal open surgery outcomes still remains uncertain in critical limb ischemia patients. The aim of this study is to evaluate the gender-specific differences in patient characteristics and long-term clinical outcomes in terms of survival, primary patency and limb salvage among patients undergoing infrainguinal open surgery for CLI.

Material and methods: All consecutive patients undergoing infrainguinal open surgery for critical limb ischemia between 2003 and 2012 were included. Survival, limb salvage and primary patency rates were assessed. Independent outcome determinants were identified by the Cox proportional hazard ratio using age and gender as adjustment factors.

Results: 584 patients (269 women and 315 men, mean age 76 and 71 years respectively) underwent 658 infrainguinal open surgery (313 in women and 345 in men). Survival rate at 6 years was lower among women compared to men with 53.5% vs 70.9% ($p < 0.001$). The same applied to primary patency (35.9% vs 52.4%, $p < 0.001$) and limb salvage (54.3% vs 81.1%, $p < 0.001$) at 6 years. Female-gender was an independent factor predicting death (hazard ratio 1.50), thrombosis (hazard ratio 2.37) and limb loss (hazard ratio 7.05) in age and gender-adjusted analysis.

Conclusion: Gender-related disparity in critical limb ischemia open surgical revascularization outcomes still remains.

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INTRODUCTION

Within the last decade, there has been an increased awareness of peripheral arterial occlusive disease (PAOD) in women, especially critical limb ischemia (CLI). Moreover, women have experienced a steady increase in cardiovascular mortality, despite improved diagnostic approaches and continuing advances in medical therapy.[1–4] It has also been demonstrated that female gender may be an independent predictor for severe and diffuse atherosclerotic disease, particularly of the femorocrural axis.[1] The common multi-level disease associated with more occlusions in women with CLI also means that lesions often require open surgery.[1]

Gender related differences in coronary artery disease or stroke have largely been studied. Evidence based gender specific treatment guidelines have already been released for coronary artery disease and cerebrovascular disease, but there are actually no guidelines concerning gender specific treatment for CLI.[2–8] Previous studies showed that women with PAOD disease had higher amputation rates and lower graft or stent patency rates after revascularization than men.[9–12] Other reports however showed similar outcomes between women and men, when adjustment for age and

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severity of disease were taken into consideration.[13–16] Unfortunately, literature analysis is difficult because of a multitude of factors that might affect outcomes, such as surgical indication (claudication, CLI), location of the disease (aorto-iliac of infrainguinal), type of intervention performed (endovascular or open surgery), type and quality of the conduit if a bypass is performed, and gender differences in patients specifically presenting with CLI remain relatively poorly studied. Nevertheless, the gender related disparity in long-term CLI outcomes has been mentioned, highlighting the need for further and longer follow up studies, and justifying the recent call to action for studies concerning women and peripheral arterial disease by the American Heart Association.[17]

In such a context, because of the diffuse and preferentially femoro-crural lesions in women, often requiring open surgery, the aim of the present study was to evaluate gender specific differences in patient characteristics and long-term clinical outcomes in terms of survival, primary patency and limb salvage among patients undergoing infrainguinal open surgery for CLI.

MATERIALS AND METHODS

Design of the study

A consecutive study of all patients who underwent infrainguinal open procedures for CLI between January 2003 and December 2012 was performed. CLI was defined as chronic ischemic rest pain or ischemic skin lesions (either ulcers or gangrene) evolving over 2 weeks, and confirmed by ankle brachial index (ABI), or transcutaneous oxygen pressure ($TcPO_2$), according to TASC II guidelines.[18] Patients presenting with infrainguinal lesions associated with supra-inguinal lesions were excluded.

Patients were retrospectively divided into two groups: men and women. Both groups were compared in terms of pre-operative, peri-operative, and post-operative parameters.

Pre-operative parameters

The following pre-operative parameters were recorded: demographics data, cardiovascular risk factors, comorbidities, surgical risk, clinical CLI status, hemodynamic measures, and number of run off arteries. Data concerning these parameters were prospectively collected in a dedicated institutional database using a data collection form specifically dedicated to CLI patients, and retrospectively analyzed.

Cardiac comorbidity was defined as congestive heart failure with ejection fraction $< 40\%$, or coronary artery occlusive disease defined as history of myocardial infarction or history of any revascularization of the coronary arteries. Renal comorbidity was defined as a creatinine clearance below 30 mL/min, and a history of stroke corresponded to cerebral comorbidity.

Surgical risk was recorded on the pre-operative anesthesia report, and defined according to the guidelines for the peri-operative cardiac management in non-cardiac surgery of the European Society of Anesthesiology.[19] High risk status patients were thus defined as patients with three or more serious comorbidities, including chronic obstructive pulmonary disease (FEV1 $< 80\%$ theoretical value), congestive heart failure (left ventricular ejection fraction $< 40\%$), coronary artery occlusive disease (defined as history of any revascularization of the coronary arteries), or chronic renal insufficiency (glomerular filtration rate < 30 mL/min/1.73 m^2).

Clinical CLI status was systematically noted pre-operatively in the data collection form, and included symptoms (rest pain or wound), wound location, wound depth, and infection. Wound depth was defined according to the Armstrong classification (grade 1, superficial ulcer; grade 2, penetrating ulcer; grade 3, ulcer penetrating to muscle, tendon, or joint articulation; grade 4, ulcer penetrating to bone).[20] Infection was defined as typical inflammatory clinical signs of infection (including foot erythema, rubor, or cellulitis) associated with a C reactive protein level > 6 mg/L, and positive local bacterial analysis.

Hemodynamic measures included ABI measurement and/or $TcPO_2$ values, and duplex ultrasound imaging.

All patients had pre-operative arteriography or computed tomography scans, and all pre-operative images were retrospectively reviewed to access the length of the lesions (according to TASC II classification) and the number of run off arteries.[1]

Surgical procedures

Types of bypasses done and types of conduits used were recorded. The policy was to carry out venous bypasses whenever possible; the suitability and quality of the vein were systematically verified pre-operatively by Duplex ultrasound imaging. The patency of all bypasses was immediately confirmed by intra-operative angiography.

Post-operative parameters

The following post-operative parameters were recorded: 30 day mortality (death within 30 days of operation), 30 day morbidity (morbidity within 30 days of operation), and post-operative length of hospital stay. Morbidity was defined as surgery related morbidity (graft thrombosis, hemorrhagic complication, operative site infection) or systemic morbidity (renal, pulmonary, cardiac or neurological failures).

The long-term follow up program consisted of clinical and hemodynamic examination with ABI or $TcPO_2$ measurements and duplex scan within 6 weeks post-operatively, at 6 and 12 months, and then annually. Patients were reviewed face to face at 6 weeks and at 6 months, and subsequently remained under angiologist supervision. Ultrasound monitoring was performed at the first check up, and then on an annual basis or even more frequently. Follow up results were analyzed in terms of survival, primary patency and limb salvage rates.

Chosen outcomes

The primary chosen outcome was long-term survival. Secondary chosen outcomes were 30 day mortality and morbidity, primary patency, and limb salvage rates.

Statistical analysis

Asymmetric quantitative variables are presented as median (MED) and interquartile range (IQR). Qualitative variables are presented as effectives and percentages.

The Fisher exact or alternatively the chi-square test, Mann–Whitney and alternatively the Student *t* tests were used to compare both groups, depending on distributions.

Log-rank tests were replaced by the Cox proportional hazard ratio adjusted for age class and sex to avoid bias in survival analysis, but also for analysis of primary patency and limb salvage rates. Cluster effects based on the Jackknife variance estimate were considered to model correlations that could appear when assessing for survival rates. The effect of age was studied by regression models and all results were adjusted for age. Relative survival rates were assessed by the ratio of the observed survival rate to the expected rate for a group of people in the general population similar to the patient group with respect to race, gender, age and calendar period of observation. Expected survival probabilities have been obtained from general French population life tables by multiplication of the published annual probabilities of survival. The appropriate probability, depending on the gender and age of the patient, and the year of registration, was obtained from the life table.

Outcome determinants were identified by the Cox proportional hazard ratio (HR) in an age and gender adjusted analysis. Variables used to perform the adjusted analysis were age, female gender, cardiovascular risk factors, surgical risk, clinical CLI status, hemodynamic measures, number of run off arteries, and types of bypasses performed. For those variables, a backward stepwise variable selection, based on level of significance, was assessed to remove redundant information. In order to account for multiple comparisons and to avoid the probability of a Type I error, the significance level was lowered at .01.

Statistical analysis was performed using R software (Language for Environment and Statistical computing, R Core team, Vienna, Austria), and SPSS (Statistical Package for Social Sciences, Chicago, USA) under the supervision of the Department of Statistics of the University.

RESULTS

Population

From January 2003 to December 2012 1,563 patients underwent surgery for CLI, and 1,094 of them presented with isolated infrainguinal lesions. Among these 1,094 patients, 510 patients underwent endovascular surgery, and 584 patients underwent open surgery (658 interventions), consisting of 269 women (313 interventions) and 315 men (345 interventions).

Pre-operative parameters

No missing pre-operative parameters were noted. Women were older than men, with a mean age of 75.8 years (median 76, IQR 10.6) for women and 70.1 years (median 71, IQR 10.0) for men ($p < .001$). Tobacco addiction was higher in the male group ($p < .001$), while comparison of other risk factors showed no difference. Both groups were comparable in terms of surgical risk and comorbidities (Table 1).

Women presented more often with bilateral disease than men: 44 (16.4%) women versus 30 (9.5%) men ($p = .01$). The proportion of patients with ulceration and rest pain was 94.2% and 5.8% for women, and 91.9% and 8.1% respectively for men, with no difference. Wound location and proportion of infections showed no difference between the groups. Wounds were deeper in men with less grade 1 and more grade 2 wounds: 88 grade 1 (29.8%) in women versus 68 (21.5%) in men ($p = .02$), and 57 grade 2 (19.3%) in women versus 88 (27.8%) in men ($p = .01$) (Table 1).

Hemodynamic measures showed no difference between groups, in terms of ABI and TcPO2 (Table 1).

In both groups, bypasses were mostly performed for TASC C and D lesions. All patients presenting with TASC A lesions had previously had endovascular treatment that had failed. Number of run off arteries showed no difference between groups (Table 1).

Surgical procedures

Comparison of bypasses done and conduits used showed no difference between both groups. Above knee femoropopliteal bypasses were performed in 69 cases (22.0%) in women and 93 cases (27.0%) in men. Below knee femoropopliteal bypasses were performed in 82 cases (26.2%) in women and 85 cases (24.6%) in men. Femorotibial bypasses were performed in 162 cases in women (51.8%) and 167 cases (48.4%) in men (Table 2).

Post-operative parameters

The 30 day mortality rates were 2.9% and 2.6% in women and men respectively, without any difference. Causes of death in women were seven acute coronary syndromes (2.3%), one massive pulmonary embolism (0.3%), and one respiratory failure due to inhalation (0.3%). Causes of death in men were six acute coronary syndromes (1.7%), two massive pulmonary embolisms (0.6%), and one septic shock after cholangitis (0.3%).

The 30 day morbidity was higher in women: 10.2% in women and 5.8% in men, $p = .04$. Causes of morbidity were 13 graft thromboses (4.2%), five acute renal failures requiring dialysis (1.6%), four acute coronary syndromes requiring stenting (1.3%), one cerebral stroke (0.3%), seven hematomas requiring re-intervention (2.2%), and two pulmonary infections (0.6%) in the female group. Causes of morbidity were four graft thromboses (1.2%), five acute renal failures requiring dialysis (1.4%), one acute coronary syndrome requiring stenting (0.3%), one pulmonary embolism (0.3%), seven hematomas requiring re-intervention (2.0%), and two pulmonary infections (0.6%) in the male group.

Mean post-operative length of hospital stay was 8.4 days for women (median 7, IQR 2), and 9.4 days for men (median 7, IQR 3), without difference between groups (Table 2).

Table 1. Pre-operative characteristics of CLI patients.

	Women group ($n = 269$) 313 interventions	Men group ($n = 315$) 345 interventions	p
Age, median (IQR)	76 years (11)	71 years (15)	<.001
Cardiovascular risk factors			
Diabetes	160 (59.5%)	187 (59.4%)	1.00
Active tobacco addiction	65 (24.2%)	244 (77.4%)	<.001
Hypertension	251 (93.3%)	285 (90.5%)	.23
Dyslipidemia	152 (56.5%)	175 (55.6%)	.87
Body Mass Index > 25 kg/m^2	92 (34.2%)	121 (38.4%)	.30
Comorbidities			
Cardiac	160 (59.5%)	181 (57.5%)	.67
Cerebral	49 (18.2%)	55 (17.5%)	.83
Renal	56 (20.8%)	58 (18.4%)	.47
High surgical risk	28 (10.4%)	28 (8.9%)	.57
CLI status			
Bilateral presentation	44 (16.4%)	30 (9.5%)	.01
Rest pain	18 (5.8%)	28 (8.1%)	.36
Ulceration	295 (94.2%)	317 (91.9%)	.36
Wound location			
Toes	169 (57.3%)	180 (56.8%)	.89
Forefoot	39 (13.2%)	48 (15.1%)	.49
Heel	16 (5.4%)	22 (6.9%)	.37
Ankle	45 (15.3%)	36 (11.4%)	.16
Calf	26 (8.8%)	31 (9.8%)	.68
Wound depth			
Grade 0	119 (40.3%)	119 (37.5%)	.48
Grade 1	88 (29.8%)	68 (21.5%)	.02
Grade 2	57 (19.3%)	88 (27.8%)	.01
Grade 3	31 (10.6%)	42 (13.2%)	.38
Wound infection	167 (56.6%)	180 (56.8%)	.97
Hemodynamic measures			
ABI, median (IQR)	0.3 (0.1)	0.3 (0.2)	.16
$TcPO_2$, median (IQR)	17 (13)	18 (14)	.75
TASC classification			
TASC A	5 (1.6%)	5 (1.4%)	.88
TASC B	31 (9.9%)	24 (7.0%)	.17
TASC C	47 (15.0%)	53 (15.4%)	.90
TASC D	230 (73.5%)	263 (76.2%)	.42
Run off arteries			
1	162 (51.8%)	187 (54.2%)	.53
2	103 (32.9%)	96 (27.8%)	.16
3	48 (15.3%)	62 (18.0%)	.37

ABI = ankle brachial index; CLI = critical limb ischemia; IQR = interquartile range; $TcPO_2$ = transcutaneous oxygen pressure.

Table 2. Surgical management of CLI patients.

	Women group ($n = 269$) 313 interventions	Men group ($n = 315$) 345 interventions	p
Type of bypass			
Above knee FP bypass	69 (22.0%)	93 (27.0%)	.14
Vein	52 (16.6%)	72 (10.9%)	.16
Prosthetic	17 (5.4%)	21 (6.1%)	.72
Below knee FP bypass	82 (26.2%)	85 (24.6%)	.65
Vein	52 (16.6%)	52 (15.0%)	.59
Prosthetic	30 (9.6%)	33 (9.6%)	.99
Femorotibial bypass	162 (51.8%)	167 (48.4%)	.39
Vein	127 (40.6%)	135 (39.1%)	.71
Prosthetic	35 (11.2%)	32 (9.3%)	.42
30 day follow up			
Mortality	9 (2.9%)	9 (2.6%)	.83
Morbidity	32 (10.2%)	20 (5.8%)	.04
Post-operative hospital stay, median (IQR)	7 days (2)	7 days (3)	.56

CLI= critical limb ischemia; FP = femoropopliteal; IQR = interquartile range.

Long-term outcomes

Mean follow up was 3.1 years (range 0.02—6 years). Observed survival rate was lower in the female group: 75.6% versus 84.1% at 2 years, 62.1% versus 76.3% at 4 years, and 53.5% versus 70.9% at 6 years, $p < .001$, adjusted $p = .008$. The relative survival rate of women was lower than for men (Fig. 1).

The primary patency rate adjusted for age and gender was lower in the female group: 61.8% versus 79.8% at 2 years, 50.9% versus 59.9% at 4 years, 35.9% versus 52.4% at 6 years, $p < .001$ (Fig. 2).

The limb salvage rate adjusted for age and gender was lower in the female group: 80.5% versus 92.7% at 2 years, 71.8% versus 88.7% at 4 years, 54.3% versus 81.1% at 6 years, $p < .001$ (Fig. 3).

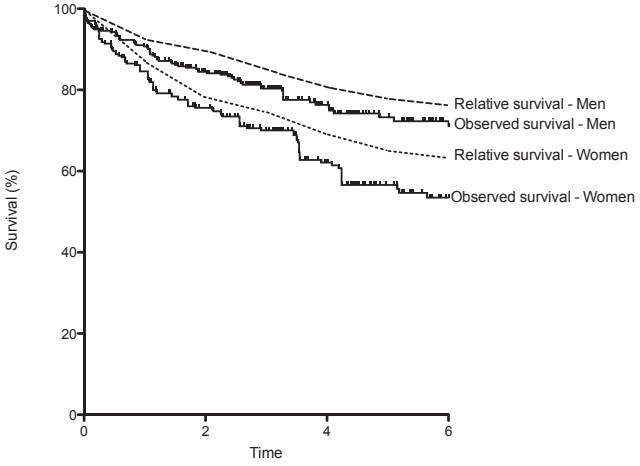
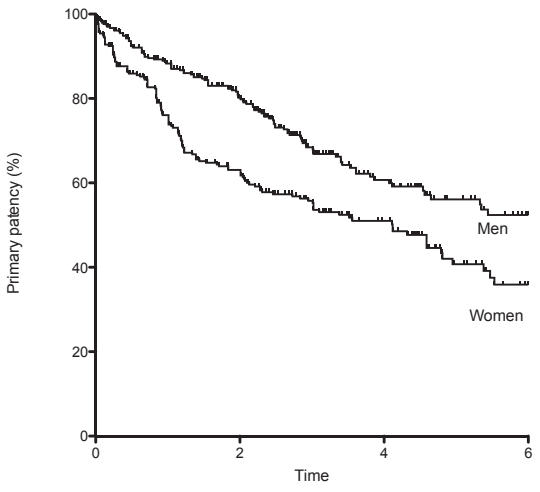


Figure 1. Survival rates.



Number at risk (year)	0	2	4	6
Men	315	200	79	37
Limbs	345	222	79	37
Women	269	123	58	19
Limbs	313	145	64	19

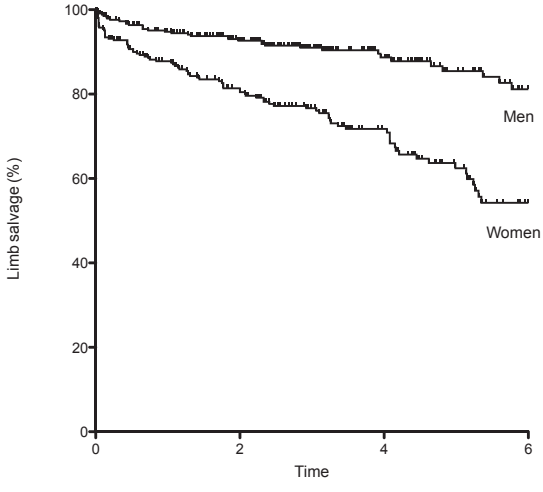
Figure 2. Primary patency rates.

Outcomes determinants

Age (HR 1.06), female gender (HR 1.50), high risk status (HR 2.30), and one run off artery (HR 1.54) appeared to be independent factors predicting death in age and gender adjusted analysis.

Age (HR 2.08), female gender (HR 2.37), high risk status (HR 2.46), grade 3 wound depth (HR 3.54), and femorotibial bypasses (venous HR 2.20, or prosthetic HR 7.13) appeared to be independent factors predicting thrombosis.

Female gender (HR 7.05), high risk status (HR 3.54), grade 3 wound depth (HR 6.91), and 1 run off artery (HR 9.04) appeared to be independent factors predicting limb loss (Table 3).



Number at risk (year)	0	2	4	6
Men	315	241	112	52
Limbs	345	251	115	58
Women	269	158	77	31
Limbs	313	184	84	31

Figure 3. Limb salvage rates.

DISCUSSION

This retrospective study evaluating infrainguinal open surgery performed in a consecutive series of CLI patients shows that female gender is a risk factor for adverse outcomes.

Most of the studies that evaluated infrainguinal revascularization in women, whether for claudication or critical limb ischemia, are retrospective analyses from single institutions.[10–12,15,16,21–24] The results of this study in terms of peri-operative mortality are similar to those already published, with no difference between women and men, and rates ranging from 2% to 3%.[11,15,21] The results in terms of peri-operative morbidity are similar to the results of all series reporting morbidity, showing a significant difference between women and men, with a higher rate of morbidity, mostly due to post-operative acute coronary syndromes in women.[11,16,21,24] In this study, 30 day morbidity in the female group also included a high incidence of graft thrombosis. A plausible explanation might be the vein and target artery characteristics, such as diameter or quality.

However, mid- and long-term gender related differences in patients affected by PAOD undergoing open surgery are reported in a conflicting way, either supporting equivalent long-term outcomes between women and men or recognizing female gender as a risk factor for adverse outcomes.[10–12,15,16,21–24] Indeed, some authors identified worse long-term outcomes in terms of survival,[10,11] patency and limb salvage,[10–12] whereas others found no difference when age adjustment or adjustment for severity were taken into consideration.[12,15,16,23,25] In this study, using age adjustment analysis, female gender appeared as risk factor for death, thrombosis and amputation. Whether these worse outcomes in the female group are only due to a

Table 3. Multivariate analysis of factors influencing survival, primary patency and limb salvage.

Overall survival	HR	95% CI	*p*
Age	1.06	1.04–1.08	<.001
Female gender	1.50	1.08–2.06	<.01
High risk status	2.30	1.50–3.51	<.001
One run off artery	1.54	0.17	<.01
Primary patency			
Age	2.08	1.40–4.39	<.01
Female gender	2.37	1.79–3.13	<.001
High risk status	2.46	1.55–3.32	<.001
Grade 3 depth	3.54	4.91–1.3	<.001
Venous FT bypass	2.20	0.95–0.98	<.01
Prosthetic FT bypass	7.13	1.59–3.02	<.001
Limb salvage			
Age	0.99	0.97–1.01	.52
Female gender	7.05	4.33–11.46	<.001
High risk status	3.54	1.54–3.94	<.01
Grade 3 depth	6.91	3.63–22.4	<.001
One run off artery	9.04	1.92–13.2	<.01

FT = femorotibial.

disadvantageous pre-operative profile, for example smaller target artery diameter, lower vein quality and worse run off, or whether gender specific patho-morphologic determinants may play a role is not clear, because not all of these factors have been examined because of the retrospective nature of the study. However, infrainguinal revascularizations were the specific focus. In some studies reporting similar outcomes between men and women, all interventions performed for CLI were included, even suprainguinal interventions. It has thus been suggested that women might have a worse outcome if the location of disease is the same as in men.[13] Moreover, it has also clearly been demonstrated that female gender may be an independent predictor for severe and diffuse atherosclerotic disease compared with men.[1]

Most of the already published studies have resulted in frequent comparisons of dissimilar patient groups, with major differences regarding incidence of diabetes or dyslipidemia, comorbidities, surgical risk, surgical indications, or surgical procedures, which could explain the widely varied conclusions of these studies. In this study, women and men were all suffering from CLI and were comparable not only in terms of cardiovascular risk factors, comorbidities, surgical risk, medications, and also in terms of location and extent of anatomical lesions (indirectly localizable by inflow sources and outflow target vessels). Types of bypasses done and types of conduits used were also similar, ensuring the technical homogeneity of both groups and the reliability of the results, especially by performing age adjusted analysis because the women were older.

The higher mean age observed in women is in accordance with previous studies, and might be due to later onset of disease, possibly resulting from the protective effects of endogenous estrogens before the menopause.[25,26] In fact, the effect of age on the outcomes of PAOD is not well understood, but patho-morphologic gender differences have also been suggested since it seems that in women after the menopause atherosclerotic disease is more rapidly progressing and more diffuse than in men.[1] It has thus been well established that PAOD is less frequent in pre-menopausal and peri-menopausal women because hormonal and metabolic factors create an athero-protective environment.[25] Moreover, the impact of menopause on increased cardiovascular risk seems to be related mainly to insulin resistance, and increased concentrations of total cholesterol and the intercellular adhesion molecule (ICAM), although the mechanisms are not well understood.[25] This could be an explanation for the poor outcomes of women in this study, although this is a hypothesis, and would require further investigation.

Another explanation of the poor outcomes of women in the study could also be related to their greater age. This may suggest that women are more likely to be referred at an older age than men and potentially treated at a more advanced stage of ischemia. The reasons for this are likely multifactorial and may include social isolation, more limited access to care for financial reasons, and CLI symptoms being mistaken for osteoporosis or arthritis, both of which are common in such patients.[23] However, in this study, pre-operative CLI presentation was the same in men and women, with a high proportion of wounds compared with rest pain in both groups. In this population, patients presenting with rest pain had a majority of TASC A and B lesions and underwent endovascular surgery first. Even when men and women presented with wounds rather than rest pain, it could be hypothesized that women had worse outcomes than men because the target artery (or vein quality) was worse, and could not deliver sufficient blood flow to allow wound healing. In women, it would thus be mandatory to adopt a prophylactic approach, in order to diagnose CLI as early as possible. Moreover, providing an intensive post-operative protocol of specific wound care and graft surveillance would be necessary.

Although the indications for immediate revascularization have been well established for CLI, in men and in women, there are to date no specific guidelines concerning management of CLI and choosing distinct treatment strategies in women.[18] However, vascular surgeons have to be aware that they could encounter more severe disease of the femorocrural arteries and diffuse atherosclerotic lesions in women.[1] Despite the conflicting reports concerning long-term outcomes of infrainguinal revascularizations in women, all reports showed higher post-operative morbidity in women, especially due to post-operative acute coronary syndromes. As women are at increased risk of post-operative cardiovascular morbidity, it would thus be critical to ensure increased post-operative monitoring. To prevent complications, a careful work up is also essential. Cardiac and respiratory status must be assessed before the procedure, and patients should be cleared by the cardiologist.

However, in this study, other factors correlate and influence outcomes more than gender, such as surgical management (especially performing prosthetic tibial bypasses) or clinical presentation (high risk status, grade 3 depth, or 1 run off artery), and the impact of female gender has to be interpreted with caution. The poor outcomes in women can be attributed to the conjunction of many factors, and worse outcomes might not be attributed to female gender alone. The notion that female gender is a risk factor for worse outcomes may be due to a misconception of “female gender” as a risk factor in itself, with high age, high risk status, often severe symptoms, and the need for distal bypasses.

The study has some limitations. First, it is a retrospective study, generating the bias linked to a retrospective data collection, even though several data were collected prospectively. Second, because many patients are increasingly treated with less invasive endovascular procedures, the data may not represent the current outcomes of all patients presenting with CLI. Furthermore, the study may have been conducted on a relatively screened group that cannot be considered as representative of the general population presenting with CLI, because it reflects a preliminary selection by physicians referring patients to the tertiary care institution. Finally, the long-term results of this population

can be difficult to analyze because of a multitude of variables that may significantly influence long-term outcomes, such as the quality of the outflow target artery or of the vein used for the bypass, post-operative wound care, or compliance with treatment, and the ability of the patient and health care team to reduce risk factors, making the role of sex on the outcomes of infrainguinal open surgery difficult to establish.

In conclusion, a gender related disparity in CLI open surgical revascularization outcomes remains. However, other factors also correlate and influence outcomes and female gender might be considered a risk factor per se, because women are more often older at presentation and present with bilateral lesions.

CONFLICT OF INTEREST

None.

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